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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,878	09/15/2006	Siegfried Ansorge	P29679	2223

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GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
10/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,878	ANSORGE ET AL.	
	Examiner	Art Unit	
	JANET L. COPPINS	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *98-117* is/are pending in the application.

4a) Of the above claim(s) *100-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *98 and 99* is/are rejected.

7)☒ Claim(s) *99* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/09, 5/5/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 98-117 are currently pending in the instant application.

Priority

2. The instant application is a 371 National Stage Entry of PCT/

Information Disclosure Statement

3. Applicants' Information Disclosure Statements (IDS), submitted November 30, 2006 and May 5, 2009, have been considered by the Examiner. Please refer to the signed copies of Applicants' PTO-1449 forms, submitted herewith.

Election/Restrictions

4. Applicant's election with traverse of Group I, claims 98 and 99, and the specific compound of "C4.002" in the reply filed on August 17, 2009 is acknowledged. The traversal is on the ground(s) that there is no serious burden on the Examiner to search all claimed inventions. This is not found persuasive because as stated in the previous Office Action, the claims herein lack unity of invention under PCT Rule 13.1 and 13.2, since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art. The compounds claimed contain an optionally substituted bicyclic (mono- or hetero-) ring system in common, which does not define a contribution over the prior art **(please note that variables are excluded)**. Attached to the instant office action is a copy of a reference that provides that the technical feature, which can be taken as a whole amongst all the alternatives, as depicted above, is not a 'special technical feature' as defined in PCT Rule 13.2, by failing to define a contribution over the prior art, as it was known in the art prior

to the filing of the instant application. Please refer to the Hashimoto et al journal article, which teaches substituted benzimidazole compounds.

Further, under "Combinations of Different Categories of Claims {Annex B, Part l(c)(I)}, Applicants are permitted a process for examination on the merits whereas Applicants are claiming several different processes. For example, treating multiple sclerosis is not the same method as treating reperfusion syndrome, or treating inflammation, since all three disorders involve different intracellular mechanisms and different treatment protocol. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

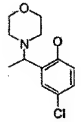
The requirement is still deemed proper and is therefore made FINAL.

5. Therefore, claims 100-117 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

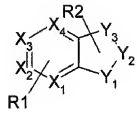
Status of the Claims

6. Claims 98-117 are pending in the instant application. Claims 100-117, as previously stated, are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions. The withdrawn subject matter is patentably distinct from the elected subject matter (i.e. a lack of unity has been found) since it differs in structure and element and would require separate search considerations. In addition, a reference, which anticipates one group, would not render obvious the other.

Applicants additionally elected the compound of "C4.002," which is a compound of C4, wherein X_1, X_2, X_3 and X_4 are each CH; Y_1 is NH; Y_2 is $C(CH_3)$; and Y_3 is CR_2; wherein R1 is H; and R2 represents a group of formula:



Therefore, the scope of the invention of the elected subject matter is as follows:



C4

Compounds of formula C4, depicted in claim 98, wherein: X_1, X_2, X_3 and X_4 are each CH; one of Y_1,Y_2 or Y_3 is NH (such that the bicyclic structure is indole or isoindole); R1 is as defined in the claims except R1 may not contain a heterocyclic or heteroaryl ring; and R2 is a heterocyclic or heteroaryl ring , or alkyl-heterocyclic or alkyl-heteoraryl ring system.

As a result of the election and the corresponding scope of the invention identified above, the remaining subject matter of claims 98 and 99, as well is 100-117 are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Accordingly claims 100-117 are withdrawn in full, as well as remaining nonelected compounds of claims 98 and 99 are withdrawn in part. The withdrawn compounds contain varying functional groups that have no elements in common other than a bicyclic carbocylic or heterocyclic

ring system, which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classification of these functional groups in the U.S. and international classification systems. Therefore the subject matter which are withdrawn from consideration as being non-elected subject matter differ materially in structure and composition and have been restricted properly and a reference that anticipates the elected compound(s) would not even render obvious the withdrawn subject matter and the fields of search are not co-extensive.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 98 and 99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds and compositions of the formula (I), including certain pharmaceutically acceptable salts thereof; the specification is not enabled for tautomers, stereoisomers, salt derivatives, or their tautomers or stereoisomes thereof, as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

> 1. the nature of the invention,

2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention is the compounds of formula C4, including all salt derivatives, tautomeric forms, stereoisomers, and pharmaceutically acceptable salts thereof.

The state of the prior art and the predictability or lack thereof in the art

Active pharmaceutical ingredients (APIs) are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact and generally stable format to store an API or a drug product. Understanding and controlling the solid-state chemistry of APIs, both as pure drug substances and in formulated products, is therefore an important aspect of the drug development process. APIs can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms such as "salt derivatives," as well as tautomers and stereoisomers of said forms are not so common as to be predictable.

With respect to isomers, any compound with the same chemical formula is an isomer of formula C4, whereas stereoisomers have the same atom to atom connectivity. Therefore, the specification would have to enable one of skill in the art how to make and use a variety of isomers, which would actually deviate from the invention.

Amount of direction/guidance & presence or absence of working examples

No direction or guidance is present for "salt derivatives" of a compound according to formula C4, or any tautomers or stereoisomers thereof, other than a brief mention of each term on pages 4 and 5 of the specification.

The disclosure fails to identify methods of preparing "salt derivatives" of the instant invention. Additionally, there are no working examples present in the disclosure for their tautomers or stereoisomers of a compound of C4 or its salts thereof. Therefore, one of skill in the art would be required to identify the correct in order to determine what is being claimed.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically: the instant claims include any tautomers, stereoisomers, salts, salt derivatives (which could include prodrugs or solvates, etc.) of a compound according to formula (I).

The quantity of experimentation necessary

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any tautomers or stereoisomers of a compound of formula C4, or its salt derivatives, tautomers or stereoisomers thereof, as instantly claimed. The science of pharmaceutical arts has

evolved such that, without guidance or working examples for said compounds in the specification, the claims lack enablement. This rejection can be overcome by deletion of the words "tautomers, stereoisomers thereof," and, "salt derivatives, tautomers and stereoisomers thereof" in the claims.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 98 rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al, IDrugs (2002). The Evans et al article teaches Dipeptidyl peptidase IV inhibitors (DPP-IV) with pharmacological utility for treating inflammation, for example. Please refer to Figure 1 on page 578, wherein several DDP-IV inhibitors are taught, specifically structure 6, which is an indole that is substituted by a substituted alkyl chain, further substituted by a heteroaryl group. As currently recited, Applicants' instant claim 98 teaches a larger genus that encompasses the species of structure 6.

11. Claim 98 rejected under 35 U.S.C. 102(b) as being anticipated by Hashimoto et al, Bioorg. Med. Chem. (2002). The Hashimoto et al journal teaches thalidomide and its derivatives that have pharmacological utility as sedatives, anti-malarial drugs, and anti-androgens. Please refer to Figure 1 on page 462 wherein several related structures are taught, specifically structures 1 and 7, which are dioxo-substituted isoindoles that are

further substituted by heterocyclic or heteroaryl groups. As currently recited, Applicants' instant claim 98 teaches a larger genus that encompasses the species of structures 1 and 7.

The Examiner recommends narrowing the scope of the claim in order to exclude the prior art references.

Claim Objections

12. Claim 99 is objected to as being dependent on rejected claim 98.

Conclusion

13. In conclusion, claims 98-117 are pending, and claims 100-117 are currently withdrawn from consideration. Claims 98 and 99 are rejected, and claim 99 is also objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JANET L. COPPINS whose telephone number is (571)272-0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Coppins/
Patent Examiner, Art Unit 1626
September 30, 2009

/Kamal A Saeed/
Primary Examiner, Art Unit 1626